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COVER

A young polar bear (*Ursus maritimus*) on a piece of ice that is drifting in the Barents Sea, northeast of Svalbard, Norway. Polar bears depend on sea ice as a platform for hunting seals, but current melting and retreat of sea ice is increasingly forcing them onto land. A recent study has found polar bears to be evolutionarily older and genetically more distinct than was previously thought. See page 344.

Photo: Florian Schulz, www.visionsofthewild.com

DEPARTMENTS

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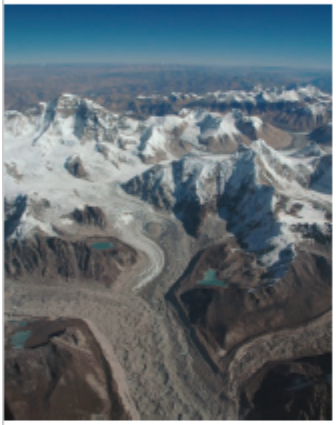

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CREDIT: (MEDIUS) KOJI FUJITA/NAGOYA UNIVERSITY

SCIENCEONLINE

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The Ancient Drug Salicylate Directly Activates AMP-Activated Protein Kinase
S. A. Hawley et al.
A possible molecular mechanism of action for a metabolite of aspirin is described.
10.1126/science.1215327

Don't Look Back in Anger! Responsiveness to Missed Chances in Successful and Nonsuccessful Aging
S. Brassen et al.
Emotionally healthy older adults show a reduced responsiveness to regret when performing a sequential decision task.
10.1126/science.1217516

Strongly Interacting Rydberg Excitations of a Cold Atomic Gas
Y. O. Dudin and A. Kuzmich
Illumination of an ensemble of cold rubidium atoms ultimately leads to high-level excitation of just a single atom.
10.1126/science.1217901

The Active Site of Methanol Synthesis over $Cu/ZnO/Al_2O_3$ Industrial Catalysts
M. Behrens et al.
Catalysis is favored by stepped copper nanoparticles decorated with zinc oxide, which promotes stronger intermediate binding.
10.1126/science.1219831

TECHNICALCOMMENTS

Comment on "Detection of Emerging Sunspot Regions in the Solar Interior"
D. C. Braun
Full text at www.sciencemag.org/cgi/content/full/336/6079/296-c

Response to Comment on "Detection of Emerging Sunspot Regions in the Solar Interior"
S. Nonidis et al.
Full text at www.sciencemag.org/cgi/content/full/336/6079/296-d

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Highlights From Our Daily News Coverage

Drugged Honeybees Do the Time Warp
General anesthesia disrupts the insect's circadian rhythm.
http://scim.ag/Drugged_Honeybees

Unhappiness Is in the Eye of the Beholder
Facial expressions not universal, as scientists once thought.
http://scim.ag/Facial_Expressions

Dangers of Chinese Medicine Brought to Light by DNA Studies
Sequencing pinpoints origins and helps reveal unknown ingredients.
http://scim.ag/Chinese_Medicine

SCIENCECAREERS

www.sciencecareers.org/career_magazine

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CAREER Q&A: From Science to Fiction
E. Ann
Spanish pharmacologist Amàlia Lafuente has written a novel about the personal and professional conflicts faced by early-career researchers.
http://scim.ag/AmaliaLafuente

Tooling Up: You Will Never Be Appreciated
D. Jensen
Scientists and other professionals can increase their job satisfaction by kicking their addiction to praise.
http://scim.ag/PraiseAddiction

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The Signal Transduction Knowledge Environment

17 April issue: http://scim.ag/ss041712

EDITORIAL GUIDE: Focus Issue—Adding Math to the Signaling Toolkit
W. Wong and J. F. Foley
Computational approaches can reveal how cells interpret, process, and respond to signals.

RESEARCH ARTICLE: Synthetic Signal Propagation Through Direct Cell-Cell Interaction
M. Matsuda et al.

PERSPECTIVE: Understanding Signaling Dynamics Through Synthesis
A. L. Slusarczyk and R. Weiss
An engineered system based on Notch and Delta in mammalian cultured cells recapitulates signal propagation, a phenomenon that occurs in development.

RESEARCH ARTICLE: Quantifying Crosstalk Among Interferon-γ, Interleukin-12, and Tumor Necrosis Factor Signaling Pathways Within a T_H1 Cell Model
D. J. Klinke II et al.
Combining experiments with mathematical modeling provides insights into the responses of T cells to cytokines.

PERSPECTIVE: Unmasking Functional Motifs Within Disordered Regions of Proteins
R. K. Das et al.
The application of a computational approach to identify short linear motifs may enable the engineering of signaling networks.

REVIEW: Computational Approaches for Analyzing Information Flow in Biological Networks
B. Kholodenko et al.
Signaling network construction and analysis provide insights into biology and medicine.

PROTOCOL: A Systematic Approach for Analysis of Peptide Array Kinome Data
Y. Li et al.
A new method of analysis of kinome data takes account of the differences between peptide arrays and DNA microarrays.

ST NETWATCH: Plant Metabolic Network (PMN)
An integrated network of researchers and data provide plant metabolic pathway models.

ST NETWATCH: Systems Biology Experiment Analysis Management System (SBEAMS)
Integrate microarray and proteomics data with a database manager and analysis package.

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18 April issue: http://scim.ag/stm041812

FOCUS: The Power of One
D. Louvard et al.
A single mouse Lgr5-positive colon stem cell can be expanded into a 3D organoid that, after transplant, contributes to the repair of injured colon epithelia in a mouse model of colitis.

RESEARCH ARTICLE: Dendrimer-Based Postnatal Therapy for Neuroinflammation and Cerebral Palsy in a Rabbit Model
S. Kannan et al.

FOCUS: A Baby Step for Nano
S. Ilan
A dendrimer-drug conjugate attenuates neuroinflammation and improves motor function in a rabbit model of cerebral palsy.
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RESEARCH ARTICLE: Patient-Specific Induced Pluripotent Stem Cells as a Model for Familial Dilated Cardiomyopathy
N. Sun et al.
Cardiomyocytes derived from iPS cells from patients with familial dilated cardiomyopathy can be used to model this disease.

RESEARCH ARTICLE: Targeted Delivery of PLK1-siRNA by ScFv Suppresses $Her2^+$ Breast Cancer Growth and Metastasis
Y. Yao et al.
Antibody-mediated delivery of anticancer small interfering RNAs suppresses $Her2^+$ breast cancer growth and metastasis.

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SCIENCE (ISSN 0036-8075) is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1200 New York Avenue, NW, Washington, DC 20005. Periodicals mail postage (publication No. 484460) paid at Washington, DC, and additional mailing offices. The title SCIENCE is a registered trademark of the AAAS. Domestic individual membership and subscription (51 issues): $149 ($74 allocated to subscription). Domestic institutional subscription (51 issues): $990; Foreign postage extra: Mexico, Caribbean (surface mail) $55; other countries (air assist delivery) $85. First class, airmail, student, and emeritus rates on request. Canadian rates with GST available upon request; GST #125439122. Publications Mail Agreement Number 1069624. Printed in the U.S.A.

Change of address: Allow 4 weeks, giving old and new addresses and 8-digit account number. Postmaster: Send change of address to AAAS, P.O. Box 96178, Washington, DC 20090–6178. Single-copy sales: $10.00 current issue, $15.00 back issue prepaid. Includes surface postage; bulk rates on request. Authorization to photocopy material for internal or personal use under circumstances not falling within the fair use provisions of the Copyright Act is granted by AAAS to libraries and other users registered with the Copyright Clearance Center (CCC) Transactional Reporting Service, provided that $30.00 per article is paid directly to CCC, 222 Rosewood Dr., Danvers, MA 01923. The identification code for *Science* is 0036-8075. *Science* is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.

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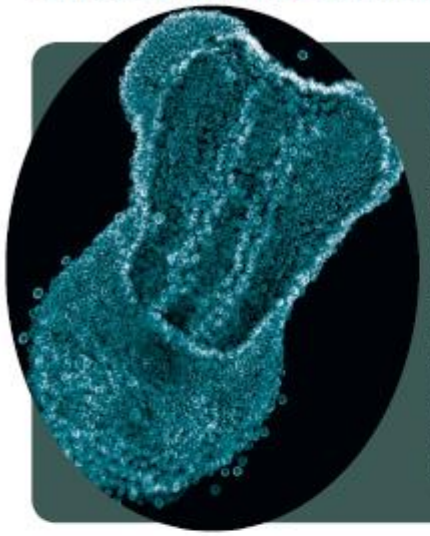
EDITED BY CAROLINE ASH AND STELLA HURTLEY



<< Tic-Toc Segmentation Clock

Molecular oscillators are an essential component of vertebrate segmentation, but whether they exist in segmented animals in general has been controversial for almost a decade. Sarrazin *et al.* (p. 338, published online 8 March; see the Perspective by Roth and Panfilio) demonstrate the existence of a segmentation clock in the growth zone of insects. Microsurgical manipulation and embryo culture revealed cyclic expression of the segmentation gene *Tc-odd* in the beetle *Tribolium castaneum*, which suggests that segmentation clocks are a widely shared mechanism that mediates animal segmentation.

Going More Slowly

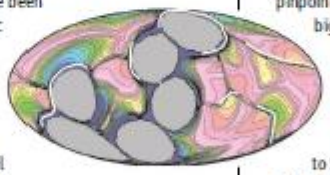
Himalayan glaciers sometimes are called the "Third Pole" because of the amount of snow and ice they contain. Despite their importance as a global water reservoir and their essential role in Asian hydrology, how their mass is changing in response to global warming is not well known. **Bolch *et al.*** (p. 310) review the contemporary evolution of glaciers in the Himalayan region, including those of the less well sampled region of the Karakoram to the Northwest, in order to provide a current, comprehensive picture of how they are changing. Most Himalayan glaciers are retreating at rates comparable to glaciers elsewhere in the world. In the Karakorum, on the other hand, advancing glaciers are more common.

Unnatural Bases

The genetic basis of all life on the planet is comprised of deoxyribonucleic acid (DNA) with four nitrogenous nucleotide bases, abbreviated to A, G, C, and T. But there are variations on this theme, and **Pinheiro *et al.*** (p. 341; see the Perspective by **Joyce**) describe the directed evolution of unnatural nucleic acid–like genetic polymers. Variant enzymes were developed that efficiently transcribed DNA to anhydrohexitol (HNA), cyclohexenyl (CeNA), locked (LNA), and threofuranosyl (TNA) nucleic acid analogs. Further variant enzymes were developed to reverse-transcribe these analogs back to DNA. Thus, man-made nucleic acid analogs can be designed and selected that have the potential to operate in a way analogous to the natural process of heredity and evolution.

Old Plates and the Sea

Estimates for the area and age of the ocean floor are at odds with assumptions for mantle convection, which imply that an older sea floor—rather than a new one—would be preferentially subducted over time. Previous efforts to explain these relationships have been based on geologic evidence and simple models. **Coltice *et al.*** (p. 335) created numerical three-dimensional convection models representing more realistic physical boundaries, including a spherical Earth, the existence of continents and supercontinents over time, and realistic rheologies. A combination of continents and plate-like behavior of the ocean floor sufficed to produce the observed relationship between plate area and plate age, which explains why some old oceanic crust still remains.



CREDITS (TOP TO BOTTOM): ANDREW D. PISS, COLTICE ET AL.

A Specific Oxidative Catastrophe

Three different classes of antibiotics induce bacterial cell death by the production of hydroxyl radicals. Hydroxyl radicals are powerful oxidizing agents in living cells and will oxidize the nucleic acid base, guanine, to form 8-oxo-guanine, which is potentially mutagenic because it can pair with both cytosine and adenine and form lethal double-strand DNA breaks. **Foti *et al.*** (p. 315) discovered that overproduction of the nucleotide sanitizer MutT, which hydrolyzes 8-oxo-dGTP to 8-oxo-dGMP, gives striking protection against cell death.

Bonded at the Source

Asymmetric catalysis is a relatively mature field in the laboratory, with a diverse array of techniques available for the selective transformation of organic compounds. However, scaling up these techniques for industrial application remains challenging, in part because many catalysts act best on reagents that have been expensively modified, although this process often generates copious waste. **Zbieg *et al.*** (p. 324, published online 22 March) combat this challenge with a ruthenium-based catalyst that couples an unmodified bulk commodity feedstock (butadiene) with alcohols, forming carbon-carbon bonds to generate complex products with high selectivity.

Hydrated in a Hurry

Water has a major influence on the conformation of proteins and related biomolecules. However, so many water molecules participate in the hydrogen bonding networks that it can be difficult to pinpoint which specific interactions play the biggest role. **Nagornova *et al.*** (p. 320) sought to answer this question for the case of a 10–amino acid ring—the antibiotic compound Gramicidin S—by probing the conformational impact of successive additions of one to 50 water molecules to the naked gas-phase structure. The primary changes in the overall ring geometry came from the addition of just the first two waters.

A Sturdy Electrode Coating

To operate efficiently, organic devices—such as light-emitting diodes—require electrodes that emit or take up electrons at low applied voltages (that is, have low work functions). Often these electrodes are metals, such as calcium, that are not stable in air or water vapor and have to be protected from environmental damage. **Zhou *et al.*** (p. 327; see the Perspective by **Helander**) report that a coating polymer containing aliphatic amine groups can lower the work functions of various types of electrodes by up to 1.7 electron volts and can be used in a variety of devices.

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